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Identification of receptor ligands with phage display peptide libraries.

Koivunen E, Arap W, Rajotte D, Lahdenranta J, Pasqualini R.

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With the development and maturation of the technology of displaying peptides on bacteriophage, it has become possible to isolate peptide ligands to various targets. In the phage display strategy, up to 10⁹ peptides of different permutations are expressed on the surface of filamentous phage. Thus, peptides capable of binding target molecules in vitro and even target tissues in vivo can be identified. In recent years, a series of libraries that display degenerate peptides of different lengths have been constructed, and specific ligands to cell surface receptors, such as integrins, have been isolated. In the in vivo biopanning, peptides targeting distinct organs or tumors have been rescued after intravenous administration of phage libraries into mice. In one application, the isolated peptide ligands have been used to direct a cytotoxic drug to tumor vasculature in mice. Further applications in radioimaging and radiotherapy are being investigated.

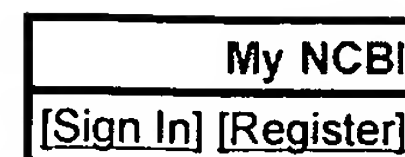
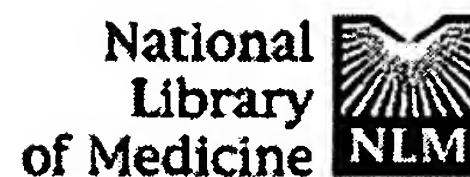
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Phage-displayed peptides mimicking the discontinuous neutralization sites of puumala Hantavirus envelope glycoproteins.

Heiskanen T, Lundkvist A, Soliymani R, Koivunen E, Vaheri A, Lankinen H.Department of Virology, University of Helsinki, Helsinki, FIN-00014, Finland.
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We selected peptide ligands mimicking the surface structure of discontinuous binding sites of Puumala hantavirus-neutralizing monoclonal antibodies from a random 18-amino acid peptide library containing a disulfide bridge in a fixed position and displayed on a filamentous phage. The varying of selection conditions, either by shortening of the association time or by competitive elution with antigen, was crucial for the selection of peptide inserts that could be aligned with the primary sequences of the envelope glycoproteins G1 and G2. Correspondingly, when the envelope glycoprotein sequences were synthesized as overlapping peptides as spots on membrane, the same site in primary structure was found as with phage display, which corroborates the use of the two methods in mapping of conformational epitopes. Also, epitopes reactive with early-phase sera from Puumala virus infection were defined with the pepspot assay in the amino-terminal region of G1. Similarities of the selected phage clones to a monoclonal antibody-escape mutant site and to a linear early-phase epitope were found. Copyright 1999 Academic Press.

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